

Attorney Docket No. 36119-125(US9)
U.S.S.N. 09/350,202

contacting a population of T cells *ex vivo* with a solid phase surface having covalently attached thereto:

- (a) a first agent which provides a primary activation signal to the T cells, thereby activating the T cells and
- (b) a second agent which stimulates an accessory molecule on the surface of the T cells, thereby stimulating the activated T cells, wherein the first agent and the second agent are covalently attached to the same solid phase surface,

the first and second agents thereby inducing the population of T cells to proliferate.

REMARKS

Claims 50-59 are pending.

Claims 56 and 59 have been canceled without prejudice as being drawn to a non-elected invention/species. Applicants reserve the right to prosecute these canceled claims in a continuation or divisional application of this Application.

Claim 50 has been amended to clarify that the first agent and the second agent are attached to the same solid phase surface. This amendment contains no new matter, as support for these amendments can be found throughout the Application, for example, at page 35, lines 9-32; and at page 36, lines 30-35. This claim amendment is not being made for a reason related to patentability. Pursuant to the provisions of 37 C.F.R. §1.121(c)(1)(ii), a marked-up version of amended claim 50 is provided herewith as Appendix A. In addition, pursuant to the provisions of 37 C.F.R. §1.121(c)(3), a copy of the claims pending following the entry of this Amendment is provided as Appendix B.

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CONCLUSION

No other fees are believed to be due in connection with this Preliminary Amendment. However, please apply any additional charges, or credit any overpayment, to our Deposit Account No. 08-0219.

Respectfully submitted,
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APPENDIX A

Marked-up Version of the Amended Claims Pursuant to 37 C.F.R. §1.121(c)(1)(ii)

50. A method for inducing *ex vivo* proliferation of a population of T cells, comprising: contacting a population of T cells *ex vivo* with a solid phase surface having covalently attached thereto:

- (a) a first agent which provides a primary activation signal to the T cells, thereby activating the T cells[;] and
- (b) a second agent which stimulates an accessory molecule on the surface of the T cells, thereby stimulating the activated T cells, wherein the first agent and the second agent are covalently attached to the same solid phase surface,

the first and second agents thereby inducing the population of T cells to proliferate.

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APPENDIX B

Claims Following Entry of this Amendment

50. A method for inducing *ex vivo* proliferation of a population of T cells, comprising: contacting a population of T cells *ex vivo* with a solid phase surface having covalently attached thereto:

- (a) a first agent which provides a primary activation signal to the T cells, thereby activating the T cells; and
- (b) a second agent which stimulates an accessory molecule on the surface of the T cells, thereby stimulating the activated T cells,

the first and second agents thereby inducing the population of T cells to proliferate.

51. The method of claim 50, wherein the first agent stimulates a TCR/CD3 complex-associated signal in the T cells.

52. The method of claim 50, wherein the first agent is an anti-CD3 antibody.

53. The method of claim 52, wherein the anti-CD3 antibody is an anti-human CD3 monoclonal antibody.

54. The method of claim 50, wherein the accessory molecule on the T cell is CD28.

55. The method of claim 54, wherein the second agent is an anti-CD28 antibody.

56. The method of claim 54, wherein the second agent is a stimulatory form of a natural ligand of CD28.

57. The method of claim 50, further comprising:
monitoring proliferation of the T cells; and

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reactivating and re-stimulating the T cells with the first and second agents when the rate of T cell proliferation has decreased to induce further proliferation of the T cells.

58. The method of claim 57, wherein the step of monitoring proliferation of the T cells is by examining cells size or determining the level of expression of a cell surface molecule, and the step of reactivating and restimulating is initiated when T cell size has decreased or when the level of the cell surface molecule has decreased.